AMENDMENTS TO THE SPECIFICATION:

Cancel the headings on page 8, lines 1 and 3 and replace them with the following new heading:

~~--Legends to figures of experiments 1-26:~~

~~Legend experiment 1:~~

Brief Description of the Drawing Figures--

Rewrite the heading on page 8, line 5, as follows:

--Fig. 1 - Experiment 1--

Cancel the heading on page 8, line 15, as follows:

~~--Legend, experiment 2:--~~

Rewrite the heading on page 8, line 17, as follows:

~~--Fig. 1~~ Fig. 2 - Experiment 2--

Cancel the headings on page 9, lines 1 and 3, and replace them with the following:

~~--Legend, experiment 3:~~

~~Fig. 1~~ Fig. 3 - Experiment 3--

Cancel the headings on page 9, lines 12 and 14, and replace them with the following:

~~--Legend, experiment 4:~~

~~Fig. 1~~ Fig. 4 - Experiment 4--

Cancel the headings on page 9, lines 23 and 25, and replace them with the following:

~~--Legends, experiment 5:~~

~~Fig. 1~~ Fig. 5a - Experiment 5--

Replace the heading on page 10, line 1, as follows:

~~--Fig. 2~~ Fig. 5b.--

Replace the heading on page 10, line 8, as follows:

~~--Fig. 3~~ Fig. 5c.--

Replace the heading on page 10, line 14, as follows:

~~--Fig. 4~~ Fig. 5d.--

Replace the headings at page 10, lines 22 and 24, as follows:

~~--Legends, experiment 6:~~

~~Fig. 1-4~~ Figs. 6a-6d.~~-~~

Replace the heading at page 11, line 21, as follows:

--Fig. [[1]] 6a.--

Replace the heading at page 11, line 26, as follows:

--Fig. [[2]] 6b.--

Replace the heading at page 11, line 30, as follows:

--Fig. [[3]] 6c.--

Replace the heading at page 12, line 1, as follows:

--Fig. [[4]] 6d.--

Replace the headings at page 12, lines 6 and 8, as follows:

~~--Legends, experiment 7:~~

~~Fig. 1-3~~ Figs. 7a-7c.~~--~~

Replace the headings at page 12, lines 19 and 21, as follows:

~~--Legends, experiment 8:~~

~~Fig. 1~~ Fig. 8a.--

Replace the heading at page 12, line 24, as follows:

--Fig. [[2]] 8b.--

Replace the heading at page 13, line 3, as follows:

--Fig. [[3]] 8c.--

Replace the headings at page 13, lines 22 and 24, as follows:

~~--Legends, experiment 9:~~

~~Fig 1~~ Fig. 9a.--

Replace the heading at page 13, line 30, as follows:

--~~Fig 2~~ Fig. 9b.--

Replace the heading at page 14, line 17, as follows:

--Fig. [[3]] 9c.--

Replace the headings at page 14, lines 23 and 25, as follows:

~~--Legend for experiment 10:~~

Fig. [[1]] 10.--

Replace the headings at page 15, lines 4 and 6, as follows:

~~--Legend, experiment 11b:~~

Fig. [[1]] 11.--

Replace the headings at page 15, lines 11 and 13, as follows:

~~--Legend, experiment 12:~~

Fig. [[1]] 12.--

Replace the headings at page 15, lines 21 and 23, as follows:

~~--Legends, experiment 13:~~

~~Fig. 1-4~~ Figs. 13a-13d.--

Replace the headings at page 16, lines 8 and 9, as follows:

~~--Legends, experiment 14:~~

Fig. [[1]] 14a.--

Replace the heading at page 16, line 18, as follows:

~~--Fig 2~~ Fig. 14b.--

Replace the headings at page 16, lines 27 and 29, as follows:

~~--Legend, experiment 15:~~

~~Fig. 1-2~~ Figs. 15a-15c.--

Replace the headings at page 17, lines 22 and 24, as follows:

~~--Legend experiment 16:~~

~~Fig.1~~ Figs. 16a-16f.--

Replace the headings at page 18, lines 13 and 15, as follows:

~~--Legend experiment 17:~~

~~Fig. 1~~ Figs. 17a-e.--

Replace the headings at page 19, lines 14 and 16, as follows:

~~--Legend, Experiment 18:~~

Fig. [[1]] 18.--

Replace the headings at page 19, lines 26 and 28, as follows:

~~--Legend experiment 19:~~

~~Fig. 1:~~ Figs. 19a-19c.--

Replace the headings at page 20, lines 11 and 13, as follows:

~~--Legend experiment 20:~~

~~Fig. 1:~~ Figs. 20a-20b.--

Replace the headings at page 21, lines 15 and 17, as follows:

~~--Legend experiment 21:~~

~~Fig. 1:~~ Figs. 21a-21c.--

Replace the headings at page 21, lines 28 and 30, as follows:

~~--Legend experiment 22:~~

~~Fig. 1:~~ Figs. 22a-22b.--

Replace the headings at page 22, lines 18 and 20, as follows:

~~--Legend experiment 23~~

~~Fig. 1:~~ Figs. 23a-23b.--

Cancel the heading at page 22, line 31 as follows:

~~--Legend experiment 24~~

Replace the heading at page 23, line 1, as follows:

~~--Fig. 1:~~ Figs. 24a-24b.--

Replace the headings at page 23, lines 16 and 18, as follows:

~~--Legend experiment 25~~

~~Fig. 1:~~ Figs. 25a-25b.--

Replace the headings at page 24, lines 14 and 16, as follows:

~~--Legend experiment 26:~~

~~Fig. 1:~~ Figs. 26a-26c.--

Please replace the paragraph beginning at page 63, line 30, with the following rewritten paragraph:

--Photos were taken after 3 days in the incubator (experiment 2, Fig. [[1]] 2).--

Replace the paragraph beginning at page 65, line 5, as follows:

--There is observed growth in all wells containing 1, 2 or 3 of the tested growth promoters. Only the well with nothing except serum in Eagles MEM showed no growth (Table 1, FIG.[[1]] 3). That indicates that normal BHK21/C13-cells will not grow in agar if there is not any extra growth stimulant present. That an analogue soft agar medium did not support growth of normal cells was first reported by MacPherson I and Montagnier L (1964) Virology 23, 291-294). The effect of conditioned medium and insulin has also been reported earlier (Tjotta E., Flikke M. and O. Lahelle (1967) Arch. ges. Virusforsh. 23, 288-291 and Tjotta E.

(1968) Arch. ges. Virusforsh. 25, 363-364), but was now adapted to this system.--

Replace the paragraph at page 65, line 25, as follows:

--Results: The results are seen in Fig. [[1]] 4, experiment 4 and summarised in Table 1:--

Replace the paragraph beginning at page 66, line 13, as follows:

--The degree of confluence of polyoma virus transformed BHK21/c13 cells, the S100T1 cell strain, growing on plastic surface was observed 2-4 days after seeding 3000 or is 110000 cells in appropriate wells of a 96 well tissue culture plate (Nunc). The dose range of 4-OH-OPB is indicated in ~~Fig. 1-4~~ Figs. 5a-5d.--

Replace the paragraph beginning at page 66, line 19, as follows:

--As shown in the pictures, about 3 times higher concentration of 4-OH-OPB is needed for total inhibition of the growth on plastic surface of the normal baby hamster kidney cell line (BHK21/c13) ~~(Fig. 3 and 4)~~ (Figs. 5c and 5d) compared to the polyoma transformed offspring ~~(Fig. 1 and 2)~~ (Figs. 5a and 5b).--

Replace the paragraph beginning at page 66, line 23, as follows:

--The experiments also show that cell density when starting is important for the effect of 4-OH-OPB. Shortening the distance to neighbour cells seems to increase the growth potential

of clones and to decrease the effect of the clonal inhibitor 4-OH-OPB ~~(Fig. 1 and 3)~~ (Figs. 5a and 5c). If this were true, cell cloning with other cells of the same kind far away would probably be inhibited most.--

Replace the paragraph beginning at page 67, line 24, as follows:

--Summary of results as demonstrated in photographs of experiment 6, ~~Fig. 1-4~~ Figs. 6a-6d.--

Replace the paragraph beginning at page 68, line 16, as follows:

--If 4-OH-OPB treatment of S100T1 started immediately after seeding, a good clonal inhibition was obtained when the concentration of 4-OH-OPB was above 1 µM. However, a delay of treatment for 24 hours only induced a small growth inhibition when adding 30 µM 4-OH-OPB, a very high dose (~~Fig 1-4~~ Figs. 6a-6d, Table 1).--

Replace the paragraph beginning at page 69, line 24, as follows:

--The experiment describes transplantation of the malignant mouse Ehrlich ascites tumour to two adult male mice (NMRI/Bom). Each of them received 100000 cells intraperitonally. One mouse was treated two times a week with 4-OH-OPB intraperitonally. After 19 days the untreated mouse was moribund (Fig. [[1]] 7a) and both were killed and examined (Fig. [[2]] 7b, experiment 7). No tumour was detected in the treated animal. The

untreated mouse, however, had about 250 millions of malignant cells in the ascitic fluid and a pea/bean sized solid tumour in the abdominal wall where the needle penetrated during transplantation (Fig. [[3]] 7c).--

Replace the paragraph beginning at page 70, line 22, as follows:

--Pictures (~~Fig 1-3~~ Figs. 7a-7c) were taken before and after death and after opening abdomen and thorax.--

Replace the paragraph beginning at page 72, line 15, as follows:

--The results are indicated in Table 2 and 3 and in ~~Fig. 1-3~~ Figs. 8a-8c of this experiment.--

Replace the paragraph beginning at page 76, line 1, as follows:

-- The clinical status and resulting ascites or tumours are described in Table 3-4 and shown in ~~Fig. 1-2~~ Figs. 9a-9b. The smallest tumour cell number necessary for growth of local tumour under the influence of 4-OH-OPB is shown in Fig. [[3]] 9c.--

Replace the paragraph beginning at page 78, line 1, as follows:

--Number 2, the untreated control, was injected with the same number of tumour cells, but had many malignant cells in the fluid (see Fig. [[1]] 9a).--

Replace the paragraph beginning at page 84, line 5, as follows:

--The cytopatogenicity of cultures that were infected with 1 µl HSV was moderate, but more pronounced in cultures with 10 µM or more of 4-OH-OPB probably as sign of toxicity (Table 1). The wells that received 1 µl HSV1 were titrated after 24 hours. 10 µM 4-OH-OPB inhibited HSV. (Table 1, Fig. [[1]] 10).--

Replace the paragraph beginning at page 85, line 16, as follows:

--The cytopatogenicity was moderate, but increased for cultures with 10 µM of 4-OH-OPB, probably caused by its toxicity (Table 1). The less cytopatogenicity of 30 µM 4-OH-OPB is not fully understood. The wells that received 2 µl HSV1 got new medium after 24 hours and were titrated after 48 hours. 1 µM 4-OH-OPB was found to inhibit satisfactorily (Table 2, FIG. [[1]] 11).--

Replace the paragraph beginning at page 87, line 8, as follows:

--The inoculated virus was removed by changing the medium the day before titration. The titration was read after 3 days and is showing a logarithmic titre loss parallel to logarithmic increase of the concentration of 4-OH-OPB that was added to the cultures Fig. [[1]] 12, ~~esperiment~~ experiment 12.--

Replace the paragraph beginning at page 90, line 21, as follows:

-- Day 3 and 4: Pictures were taken of the 6 wells. It is evident that only the control shows clonal growth at a certain distance from the central cell mass. This central mass seemed to

grow at about the same rate in all wells. But the growth difference was easily observed between the control and wells with inhibitor where the cell density was low (~~Fig. 1-4~~ Figs. 13a-13d, Table 5-6).--

Replace the paragraph beginning at page 95, line 7, as follows:

--The lowest inhibiting dose of 4-OH-OPB that inhibits the growth of clones of MT4 cells in a cell culture with fluid medium was found (Fig. [[1]] 14a). The concentration of 4-OH-OPB needed for arresting colony growth was about 2 logs less in MT4 cultures with 5000 cells than in cultures with 500000 cells (Fig. [[2]] 14b). The interpretation of this is probably not that each cell needed a certain amount 4-OH-OPB to be bound to postulated receptors of the cell for full clonal inhibition, since in agar cultures seeded with cells in a concentration gradient, the colony inhibition was strongest in sparsely seeded areas.--

Replace the paragraph beginning at page 100, line 4, as follows:

--As shown in ~~Fig. 1-2~~ Figs. 15a-15c, experiment 15, 4-OH-OPB was inhibiting clonal growth at the concentrations tested, 2 and 20 µM.--

Replace the paragraph beginning at page 108, line 20, as follows:

--The control 4-OH-OPB was clearly better than any other. See Figs. 16a-16f.--

Replace the paragraph beginning at page 113, line 13, as follows:

--Discussion and Conclusion: None of the tested inhibitors (Colchicine, Podophyllotoxin, or Etoposide) did inhibit clonal cell growth as effectively as 4-OH-OPB (Table 7-8). All three seemed to allow the growth of a few small clones in sparsely seeded locations of the agar (~~Fig. 1~~ Figs. 17a-17e, experiment 17).-- /

Replace the paragraph beginning at page 114, line 11, as follows:

--Thus, the tested growth inhibitors consisted of two groups, the inhibitors that inhibited cell growth in both high and low cell density locations, the Podophyllotoxin group, and the inhibitors that only inhibited clonal growth in low density areas, 4-OH-OPB and Colchicine. Especially for average 4-OH-OPB concentration there is good growth of colonies in high-density areas, but no growth in low-density areas (Table 7, ~~Fig. 1~~ Figs. 17a-17e).--

Replace the paragraph beginning at page 119, line 15, as follows:

--The answer of the last question: "Will Colchicine alone stop settlement of transplanted Ehrlich tumour cells when mixing the drug with the transplanted cells before injecting them as done with 4-OH-OPB?" is also NO. The concentrations, thought to be quite high, did not provide complete protection against the

development of transplantable Ehrlich tumour Table 1, Fig. [[1]] 18).--

Replace the sentence following the asterisk at the end of Experiment 19, Table 1 on page 127, line 15, as follows:

--If solved in 20 litres extracellular fluid of a man of 70 kg. The concentrations in experiment, see ~~Fig. 1~~ Figs. 19a-19c.--

Replace the paragraph beginning at page 127, line 16, as follows:

--Results after 48 hours incubation using high, medium or low concentration of the ~~compunds~~ compounds tested are shown in ~~Fig. 1~~ Figs. 19a-19c and summarised in Table 2.--

Replace the paragraph beginning at page 132, line 1, as follows:

--Low cell numbers are easily inhibited to grow. But the control shows much better growth in sparsely seeded areas than in treated cultures. Therefore, the treatment is to be blamed for the specific growth inhibition in sparsely seeded areas (~~Fig. 1~~ Figs. 20a-20b).--

Replace the paragraph beginning at page 134, line 1, as follows:

--Fluorouracil showed a relatively moderate clonal inhibition and low toxicity. The effect was not dependent on concentration within the range tested. See Figs. 21a-21c.--

Replace the paragraph beginning at page 135, line 21, as follows:

--This time the growth in dense areas of the control 4-OH-OPB was absent in high concentration of the inhibitor and doubtful in medium concentration (Table 2, ~~Fig. 1~~ Figs. 22a-22b).--

Replace the paragraph beginning at page 139, line 9, as follows:

--The control, the clone inhibitor 4-OH-OPB, showed some inhibition of total growth in densely seeded areas of the soft agar culture when added in high or medium concentrations (~~Fig. 2~~ Figs. 23a-23b, Table 2). However, clonal growth was present even in wells with high concentrations of the compound, but only in densely seeded areas. All wells with this compound showed complete inhibition of clonal growth in sparsely seeded areas.--

Replace the paragraph beginning at page 139, line 14, as follows:

--The compound #2: 2-Butyl-2-hydroxy-N-(4-hydroxy-phenyl)-N'-phenyl malonamide and probably also #1, p-hydroxy-azobenzene had an effect very similar to 4-OH-OPB, but at at least 66 times higher concentration (Table 2, ~~Fig. 1~~ Figs. 23a-23b). They showed an effective clone inhibition selectively in sparsely seeded areas of the polyoma virus transformed cells S100T1 in soft agar cultures for high concentrations of the compounds. The

possibility of using these two analogues in treatment of diseases would very much depend on toxicological factors.--

Replace the paragraph beginning at page 141, line 7, as follows:

--None of the analogous compounds to 4-OH-OPB tested, list number 5, 8 and 9 (Table 1), did show significant inhibition of clonal growth (Table 2, ~~Fig. 1~~ Figs. 24a-24b). In this experiment the control, 4-OH-OPB, showed reduced clonal growth in the densely seeded areas of high or medium concentrations (9 and 3 µM). Clonal growth, however, was significantly inhibited in the concentration range 9 to 0.33 µM. The effect was gone at 0.11 µM.--

Replace the paragraph beginning at page 143, line 4, as follows:

--Azathioprine: 2 tablets of 25 mg each were solved in distilled water and sterile filtered. It was relevant also to test lower dilutions of 4-OH-OPB than done before (~~Fig. 1~~ Figs. 25a-25b).--

Replace the paragraph beginning at page 144, line 12, as follows:

--Next: Use of Somatotropine on these cells seemed to create some large colonies. But other wells with other substances added might have large colonies too. Other pictures might not show big colonies because they were all rare. Therefore, the large

colonies could be, but may not be specific for this hormone (~~Fig. 1~~ Figs. 25a-25b, Table 2).--

Replace the paragraph beginning at page 147, line 15, as follows:

--The results were read after 24 hours. The 4-OH-OPB showed nice and complete inhibition for high and medium concentrations on sparsely seeded cells (~~Fig. 1~~ Figs. 26a-26c, Table 2). Low concentration showed break through of clonal growth close to the sparsely seeded limit in the right hand side of the picture. High concentration did not affect the densely seeded parts of the gradient, which might indicate a low toxicity for densely collocated cells. It is our opinion that these cells were analogous to most of the organs in the organism and would indicate organ toxicity in the body. However, after storing 4-OH-OPB solved in DMSO in the refrigerator, a cytotoxic effect had occasionally been observed of high concentrations added to densely seeded S100T1 cells. This is important since in treatment of patients, only toxic or growth-inhibiting effect on sparsely seeded cells is desired.--

Replace the paragraph beginning at page 148, line 9, as follows:

--The carcinogenic Benzo(a)pyrene in high dose gave increased clonability (~~Fig. 1~~ Figs. 26a-26c, Table 2). This phenomenon is believed to relate to the carcinogenic effect of the compound. Sulindac showed both a weak anti-cloning effect on

sparsely seeded cells when adding high dose and a clone-inducing effect on the same cell density if the added dose was low. Low dose seemed also to increase growth in densely seeded areas of the same well. No effect on cell growth was observed when adding Altretamine.--